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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/681,388	10/07/2003	John H. Kenten	IGN-2005US03	7445

7590 03/09/2007
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EXAMINER

HISSONG, BRUCE D

ART UNIT PAPER NUMBER

1646

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No. 10/681,388	Applicant(s) KENTEN ET AL.	
	Examiner Bruce D. Hissong, Ph.D.	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 December 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 86 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 86 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Formal matters

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/11/2006 has been entered.

2. Claim 86 is currently pending and is the subject of this office action.

Claim Objections

1. Objection to claim 86 regarding the phrase "two of more", as set forth on page 3 of the office action mailed on 7/11/2006, is withdrawn in response to Applicants' amendments to the claim to recite "two or more".

2. Objection to claim 86 regarding the phrase "selected form", as set forth on page 3 of the office action mailed on 7/11/2006, is withdrawn in response to Applicants' amendments to the claim to recite "selected from".

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Rejections withdrawn

1. Rejection of claim 86 under 35 USC § 112, second paragraph, as being indefinite regarding whether the antibody to be detected recognizes epitopes from parts *i – iv*, or just part *iv*, as set forth on page 5 of the prior office action mailed on 7/11/2006, is withdrawn in response

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to Applicants' amendment to the claim to recite "wherein one or more epitopes of steps (a)(i) – (a)(iv) are recognized by the antibody to be detected.

2. Rejection of claim 86 under 35 USC § 112, second paragraph, as being indefinite regarding lack of antecedent basis for the term "the ubiquitin protein", as set forth on page 4 of the prior office action mailed on 7/11/2006, is withdrawn in response to Applicants' amendment to the claim to recite "the ubiquitin protein".

Rejections maintained

3. Claim 86 remains rejected under 35 USC § 112, second paragraph, as being indefinite regarding the recitation of an "ubiquitin fusion protein comprising ubiquitin fused to a single epitope-containing segment", followed by "the epitope-containing segments" as set forth on pages 4-5 of the prior office action mailed on 7/11/2006. Furthermore, the claim was also found to be indefinite in regards to the recitation of "fusion sites selected from the groups", while the claim only contained a single group from which to select fusion sites.

In the response received on 12/11/2006, the Applicants argue that the claim has now been amended to recite "epitope-containing segments" and "fusion sites selected from the group", and therefore the amended claim is not indefinite. However, it is noted that the claim has been amended to recite "epitope-containing segment[s]" and "fusion sites selected from the group[s]". It is not clear if the recitation of "segment[s]" and "group[s]" means "segment or segments" or "group or groups" respectively, or if the "[s]" is meant as a deletion or addition of the character "s" to the claims.

4. Claim 86 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Part (a)(iii) of claim 86 recites a ubiquitin fusion protein, wherein the fusion site for said fusion protein is selected from the group consisting of the C-terminus wherein said fusion site is non-cleavable, the N-terminus, or an internal fusion site. However, part (a)(iv) is drawn to a ubiquitin fusion protein with a fusion site at the C-terminus, wherein said fusion site is non-cleavable or the N-terminus of the ubiquitin protein. Because part (a)(iv) specifically recites the N-terminus of the ubiquitin protein, it is not clear if the fusion sites of part (a)(iii) are also drawn to the C- or N-terminus, or internal site of the ubiquitin protein, or some other protein.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claim 86 remains rejected under 35 USC § 102(b) as being anticipated by Vannier *et al* ("Vannier"), as set forth on pages 5-7 of the office action mailed on 7/11/2006, and pages 6-7 of the office action mailed on 10/18/2005.

In the response received on 12/11/2006, the Applicants argue that the claim as currently amended, has two limitations that are not taught by Vannier. First, the claim has been amended to recite a ubiquitin fusion protein comprising two or more identical epitopes, wherein the two or more identical epitopes are located on one or more epitope containing segments. The Applicants argue that it is highly unlikely that the ubiquitin-FSHR fusion protein taught by Vannier possesses two or more identical epitopes. Second, the claim now recites a ubiquitin fusion proteins wherein the fusion site is selected from one of three sites, including the C-terminus wherein said fusion site is non-cleavable. The Applicants assert that the fusion site for the fusion protein of Vannier is located at the C-terminus, but is cleavable.

These arguments have been fully considered and are not persuasive. The Examiner agrees that the protein of Vannier is unlikely to have two or more identical epitopes, as recited in parts (a)(i) and (a)(ii). However, the language of the claim is such that the ubiquitin fusion protein can be selected from any of parts (a) (i – iv). Parts (a)(iii) and (a)(iv) specifically recite a ubiquitin fusion protein with a fusion site that can be at the C-terminus, wherein said fusion site is non-cleavable. Vannier is silent regarding whether or not the fusion site of the ubiquitin-FSHR fusion protein is cleavable, and the Applicants have presented no evidence supporting the assertion that it is cleavable. As stated in the previous office actions, the USPTO does not have the facilities for testing the ubiquitin-FSHR fusion protein of Vannier, and the burden is on the Applicant to show that the fusion protein taught by Vannier would indeed be cleavable at the site of ubiquitin-FSHR fusion. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.). Therefore, for these reasons and the fact that parts (a)(iii) and (a)(iv) recite a fusion protein comprised of one or

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more identical or non-identical epitopes, and the fusion protein of Vannier would be expected to comprise one or more non-identical epitopes, the disclosure of Vannier meets the limitations of parts (a)(iii) and (a)(iv).

2. Claim 86 remains rejected under 35 USC § 102(b) as being anticipated by Loosfelt *et al* ("Loosfelt"), as set forth on pages 7-8 of the office action mailed on 7/11/2006, and page 7 of the office action mailed on 10/18/2005.

In the response received on 12/11/2006, the Applicants argue that the claim as currently amended, has two limitations that are not taught by Loosfelt. First, the claim has been amended to recite a ubiquitin fusion protein comprising two or more identical epitopes, wherein the two or more identical epitopes are located on one or more epitope containing segments. The Applicants argue that it is highly unlikely that the ubiquitin-TSHR fusion protein taught by Loosfelt possesses two or more identical epitopes. Second, the claim now recites a ubiquitin fusion proteins wherein the fusion site is selected from one of three sites, including the C-terminus wherein said fusion site is non-cleavable. The Applicants assert that the fusion site for the fusion protein of Loosfelt is located at the C-terminus, but is cleavable.

These arguments have been fully considered and are not persuasive. The Examiner agrees that the protein of Loosfelt is unlikely to have two or more identical epitopes, as recited in parts (a)(i) and (a)(ii). However, the language of the claim is such that the ubiquitin fusion protein can be selected from any of parts (a)(i – iv). Loosfelt is silent regarding whether or not the fusion site of the ubiquitin-TSHR fusion protein is cleavable, and the Applicants have presented no evidence supporting the assertion that it is cleavable. As stated in the previous office actions, the USPTO does not have the facilities for testing the ubiquitin-TSHR fusion protein of Loosfelt, and the burden is on the Applicant to show that the fusion protein taught by Loosfelt would indeed be cleavable at the site of ubiquitin-TSHR fusion. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.). Therefore, for these reasons and the fact that parts (a)(iii) and (a)(iv) recite a fusion protein comprised of one or more identical or non-identical epitopes, and the fusion protein of Loosfelt would be expected to comprise one or more non-identical epitopes, the disclosure of Loosfelt meets the limitations of parts (a)(iii) and (a)(iv).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 86 is rejected under 35 U.S.C. 103(a) as being unpatentable over either Vannier or Loosfelt. The instant invention is drawn to a method of detecting the presence of specific antibodies in a sample, comprising providing a ubiquitin fusion protein, a sample suspected of comprising antibodies reactive with the ubiquitin fusion protein, forming an incubation mixture comprising the ubiquitin fusion protein and the experimental sample, and detecting antibodies in the sample. As set forth in the previous office actions mailed on 10/18/2005, and 7/11/2006, Vannier and Loosfelt teach methods of detecting antibodies, wherein said method comprises providing a ubiquitin-FSHR fusion protein, or a ubiquitin-TSHR fusion protein, respectively. Furthermore, the method steps of the methods taught by Vannier and Loosfelt are identical to those of the instant application. Although neither Vannier nor Loosfelt teach a ubiquitin fusion protein that meets the limitations of part (a)(i) and (a)(ii), it would be obvious to one of ordinary skill in the art to create such fusion proteins and use them in a method of detecting antibodies. The motivation to do so comes from the fact that both Vannier and Loosfelt teach that specific antibodies can be detected in methods comprising use of ubiquitin fusion proteins, and that creation of fusion proteins is well-known and routine in the art. Thus, by routine experimentation, one of ordinary skill in the art could create ubiquitin fusion proteins comprised of any antigen, epitope, or epitopes, and use the fusion proteins in methods of detecting specific antibodies. For these reasons, the instant invention is obvious in view of either Vannier or Loosfelt.

Conclusion

No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571) 272-3324.

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The examiner can normally be reached M-F from 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D., can be reached at (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BDH
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A handwritten signature in black ink, appearing to read "Gary B. Nickol". The signature is written in a cursive, flowing style.

GARY B. NICKOL, PH.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600